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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,445	11/16/2001	Ernest G. Schutt	ALLIA.62F1C1C1	3983
48394	7590	05/03/2005	EXAMINER	
NORTON & DIEHL, LLC 77 BRANT AVE SUITE 110 CLARK, NJ 07066			SHARAREH, SHAHNAME J	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/991,445

Applicant(s)

SCHUTT ET AL.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/28/2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 12-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/28/2004.

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 28, 2004 has been entered.

2. Applicant has made an election of species on the Paper filed on July 2003. Accordingly, perfluorobutane was elected as the species for fluorocarbons and oxygen was elected as the species for the modifier gas. Claims 1-10, 12-20 read on the elected species and are pending.

Applicant's arguments filed on December 28, 2004 have been fully considered but are now moot in view of new grounds of rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-10, 12-20 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of 1-12 of US Patent 6,372,195, claims 1-101 of US Patent 6,258,339, claims 1-24 of US Patent 5,695,741, claims 1-38 of US Patent 5,639,443, and claims 17-22 of US Patent 5,798,091, claims 1-9, 38-73 of US Patent 5,804,162, claims 26-51 of US Patent 6,193,952 for the reasons or record

Applicant's request to revisit this rejection after the claims have been formally allowed is noted.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 depends on the canceled claim 11. Clarification of dependency is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-10, 13-18, 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Schneider US Patent 5,413,774.

The instant claims are directed microbubbles comprising at least one fluorocarbon gas and at least one modifier gas that can comprise oxygen. The scope of the instant limitation "modifier gas" is described in paragraphs 0034, 0061-0069. Accordingly, the scope of the term "a modifier gas" is inclusive and encompasses other gases such as oxygen, air, perfluorocyclooctane, perfluoropentane, perfluoroethane and perfluoromethane.

Further, the instant limitation "physiological gases surrounding external medium" such as blood, or "physiological gas present in the surrounding external medium" such as oxygen and air, recited in claims 3, 5-8, 10, 12-13, 17-19 are not viewed to positively limit the claimed microbubbles because they are not recited in a manner limiting the structural elements of the instantly claimed microbubbles. Accordingly, mere presence of any microbubbles in blood would meet such limitations.

Schneider anticipates the limitations of the claimed microbubbles. Schneider teaches gas filled microvesicles that can contain a mixture of a first perfluorocarbon gas such as perfluorobutane (C₄F₁₀) and a secondary gas such as air which contains oxygen, nitrogen, CO₂. (see col 5, lines 50-56., examples 7-8*, claims 1-2, col 14, lines 45, 68). The second gas of Schneider can include other perfluorocarbons such as perfluoromethane or perfluoroethane. (see (col 14, lines 42-49). Schneider also teaches a membrane around his microvesicles (see claims 5-9).

Schneider's fluorocarbon is the same as those instantly claimed, therefore, it inherently possesses the same functional characteristics as the instant fluorocarbon.

Air, nitrogen and the like gases including other perfluorocarbons also fall within the instant genus of modifier gases. Thus, the microbubbles of Schneider contains a perfluorobutane. The microbubbles of Schneider also comprise a secondary gas including air, perfluoromethane, which meets the instant limitation "modifier gas."

Schneider's microbubbles comprise a membrane comprising phospholipids or albumin. (see col 13-14). Schneider administers his microvesicles to Rabbits thus exposing them to an external medium comprising blood and other physiological gases such as air or oxygen. (see examples 2-4, cols 9-11). Thus, Schneider meets all structural limitations of the instant claims and subsequently anticipates all functional limitations of the instant claims as well.

6. Claims 1-10, 12-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Lambert et al US Patent 5,552,133.

Lambert teaches encapsulated gaseous microspheres comprising gaseous mixtures wherein the gases are selected from the group perfluoroethane, perfluoropropane, perfluorobutane, oxygen, nitrogen and air. (see col 4, lines 59-col 5, line 10; col 7, lines 35-col 9, line 20). Lambert's microspheres also comprise a membrane made of albumin. (see abstract, col 9, lines 1-21). Since Lambert's microspheres meets all structural limitations of the instant claims, they are inherently capable of performing the claimed functional limitations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
7. Claims 12, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al US Patent 5,413,774 in view of Tickner US Patent 4,265,251.

The teachings of Schneider are described above. Schneider only fails to incorporate delivery of oxygen in his microbubbles.

Tickner teaches methods of ultrasound imaging using gas containing microbubbles wherein the gas is oxygen (abstract, col 7, lines 11-54). Tickner teaches that although the preferred gas is carbon dioxide, however, other gases such as freons and oxygen may be used in his contrast agents (col 6, lines 63-67)..

Although Schneider fails to use oxygen with pefluorobutane in his gaseous mixtures compositions, he specifically teaches that any gas like air and nitrogen can be

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employed in his gaseous mixture. Tickner shows that for the purposes of ultrasonic contrast agents, gases such as oxygen, nitrogen, and Freons are substantially interchangeable and are functional equivalents.

Thus, absence of showing unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to substitute one of air or nitrogen gases in Schneider's microvesicles with oxygen and create a microvesicle tha contains pefluorobutane and oxygen, because as shown by Tickner, oxygen is considered art recognized equivalents to suitable gases enumerated by Schneider. Subsequently, the ordinary skill in the art would have had a reasonable expectation of success in mixing perfluorobutane with oxygen to produce a gaseous microvesicles.

8. Claims 12 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider in view of Unger US Patent 5,205,290.

The teachings of Schneider are described above. Schnedder does not specifically uses oxygen in his gaseous mixture.

Unger teaches contrast agents comprising gaseous microspheres containing oxygen. (see abstract; col 5, lines 10-25, claim 8). Unger also teaches the use of volatile liquids having low boiling points within his microspheres to allow expansion of the microspheres (see col 4, lines 9-58). Unger specifically teaches the use of perfluorocarbons such as those having between 1 and about 9 carbon atoms especially C₄F₁₀ (perfluorobutane). Accordingly, Unger teaches the *in vivo* administration of oxygen and perfluorobutane as gas expanding compounds within the microspheres of

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his contrast agents. Unger, however, fails to use his compositions for ultrasound imaging.

Nevertheless, it would have been obvious to one of ordinary skill in the art at the time of invention to utilize a mixture of a suitable perfluorocarbons such as perfluorobutane, as taught by Schneider, and oxygen, as taught by Unger, because the ordinary skill in the art would have had a reasonable expectation of success in preparing a gaseous microbubble for therapeutic or diagnostic use. Absence of showing unexpected results, one of ordinary skill in the art would have had a reasonable expectation in observing similar properties when mixing perfluorobutane of Schneider with oxygen of Unger for use ultrasound imaging.

Conclusion

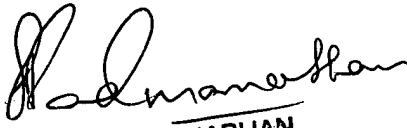
9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SS


SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER